K081193

Attachment 5

JAN 16 2009

510(k) Summary – COBAS INTEGRA 400/800 Bilirubin Total

Introduction

According to the requirements of 21 CFR 807 92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence

Submitter name, address, contact

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Date prepared April 23, 2008

Device Name

Proprietary name Cobas Integra 400/800 Bilirubin Total
Common name Bilirubin (total or direct) test system
Classification name Bilirubin (total or direct) test system

Device Description

The Cobas Integra Bilirubin Total reagent is intended for use with the Cobas Integra systems for the quantitative determination of the total bilirubin concentration in human serum

Intended use

In vitro test for the quantitative determination of the total bilirubin concentration in human serum on Cobas Integra Bilirubin is formed in the reticuloendothelial system during the degradation of aged erythrocytes The heme portion from hemoglobin and from other heme-containing proteins is removed, metabolized to bilirubin and transported as a complex with serum albumin to the liver In the liver, bilirubin is conjugated with glucuronic acid for solubilization and subsequent transport through the bile duct and elimination via the digestive tract Diseases or conditions which, through hemolytic processes, produce bilirubin faster than the liver can metabolize it, cause the levels of unconjugated (indirect) bilirubin to increase in the circulation Liver immaturity and several other diseases in which the bilirubin conjugation mechanism is impaired cause similar elevations of circulating unconjugated bilirubin Bile duct obstruction or damage to hepatocellular structure causes increases in the levels of both conjugated (direct) and unconjugated (indirect) bilirubin in the circulation

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Predicate Device

We claim substantial equivalence to the Cobas Integra Bilirubin Total (K951595)

Substantial equivalency – device comparison

The table below indicates the similarities and differences between the modified Bilirubin Total and the predicate Bilirubin Total (K951595)

Characteristic	Predicate Cobas Integra Bilirubin Total (K951595)	Modified Cobas Integra Bilirubin Total
Intended Use	The Cobas Integra Cassette Bilirubin Total (BIL-T) contains an in vitro diagnostic reagent system intended for use on Cobas Integra for the quantitative determination of the total bilirubin concentration in serum and **plasma** (test BIL-T, 0-048)	In vitro test for the quantitative determination of the total bilirubin concentration in human serum (test BIL-T, 0-048) on Cobas Integra
Indications for Use	Bilirubin is formed in the reticuloendothelial system during the degradation of aged erythrocytes The heme portion from hemoglobin and from other heme-containing proteins is removed, metabolized to bilirubin and transported as a complex with serum albumin to the liver In the liver, bilirubin is conjugated with glucuronic acid for solubilization and subsequent transport through the bile duct and elimination via the digestive tract Diseases or conditions which, through hemolytic processes, produce bilirubin faster than the liver can metabolize it, cause the levels of unconjugated (indirect) bilirubin to increase in the circulation Liver immaturity and several other diseases in which the bilirubin conjugation mechanism is impaired cause similar elevations of circulating unconjugated bilirubin Bile duct obstruction or damage to hepatocellular structure causes increases in the levels of both conjugated (direct) and unconjugated (indirect) bilirubin in the circulation	Same

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Characteristic	Predicate Cobas Integra Bilirubin Total (K951595)	Modified Cobas Integra Bilirubin Total
Assay principle	Diazo method	Same
Active Ingredients	R1 R2 Test Sulfanilic Acid 35 13 5 mmol/L Oxalic Acid 40 15 4 mmol/L HEDTA 4 1 5 mmol/L Myristytrimethyl-ammonium bromide 2 0 8 % Dodecyltrimethyl-ammonium bromide 5 1 9 % Sodium nitrite 24 5 3 1 mmol/L pH 1 1 6 8 1 4	Same
Measuring range	Test range 0-340 umol/L (0-20 mg/dL) w/postdilution 0-1020 umol/L (0-60 mg/dL) Postdilution factor 3	1 7 – 340 umol/L (0 099-20 mg/dL) Determine samples having higher concentrations via the rerun function Dilution of samples via the rerun function is a 1 3 dilution Results from samples diluted by the rerun function are automatically multiplied by a factor of 3
	Sensitivity The sensitivity is defined as the change of analytical response (ΔA) per unit change in analyte concentration at a pathlength of 1 cm The sensitivity is 2 9 x 10^{-3} ΔA per umol/L of total bilirubin (5 0 x 10^{-2} ΔA per mg/dL of bilirubin)	Lower Detection Limit 1 7 umol/L (0 099 mg/dL) The detection limit represents the lowest measurable analyte level that can be distinguished from zero It is calculated as the value lying three standard deviations above that of a zero sample (zero sample + 3 SD, within-run precision, n=30)

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Characteristic	Predicate Cobas Integra Bilirubin Total (K951595)	Modified Cobas Integra Bilirubin Total
Precision	Precision was evaluated on Cobas Integra using two human serum pools and following the guidelines of the NCCLS Manual EP5-T2 Level 1 / Level 2 Mean 24 2 umol/L (1 4 mg/dL) / 72 5 umol/L (4 2 mg/dL) CV w/in run 0 46% / 0 45% CV day/day 0 48% / 0 53% CV total 0 78% / 0 80%	Reproducibility was determined using human samples and controls in an internal protocol (within-run n=20, between-run n=20) The following results were obtained Level 1 / Level 2 Mean 24 2 umol/L (1 4 mg/dL) / 72 5 umol/L (4 2 mg/dL) CV w/in run 0 46% / 0 45% CV total 0 78% / 0 80%
Accuracy	Accuracy Total bilirubin values for human sera and plasma samples obtained on Cobas Integra with the cassette bilirubin total were compared to those determined with reagents for total bilirubin on Cobas Mira and the commercially available alternative clinical chemistry system Samples were measured in duplicate Sample size (n) represents all replicates Values ranged from 1 7 to 350 6 umol/L (0 1 to 20 5 mg/dL) Cobas Mira Sample size (n) 208 Corr Coefficient (r) 0 999 (r_s) 0 985 Lin Regression y=1 00x + 1 2 umol/L Passing Bablock y=1 00x + 0 6 umol/L Alternative System Sample size (n) 210 Corr Coefficient (r) 0 999 (r_s) 0 972 Lin Regression y=0 93x + 0 8 umol/L Passing Bablock y=0 93x + 0 4 umol/L	Method Comparison Total bilirubin values for human serum samples obtained on a Cobas Integra 800 analyzer using the Cobas Integra Bilirubin Total reagent (y) were compared to those determined using Cobas Integra Total Bilirubin Special reagent on a Cobas Integra 800 analyzer (x) Cobas Integra 800 analyzer Sample size (n) = 49 Passing/Bablok y=0 956x + 2 113 umol/L r=0 999 Values ranged from 5 49 to 317 umol/L (0 321 to 18 5 mg/dL) Total bilirubin values for human serum samples obtained on a Cobas Integra 400 analyzer using the Cobas Integra Bilirubin Total reagent (y) were compared to those determined with commercially available reagents for total bilirubin on a Roche/Hitachi 911 analyzer (x) Roche/Hitachi 911 analyzer Sample size (n) = 104 Linear regression y=0 989x – 0 520 umol/L r= 0 999 Passing/Bablok y= 0 991x + 0 219 umol/L Values ranged from 3 29 to 282 umol/L (0 192 to 16 5 mg/dL)

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Characteristic	Predicate Cobas Integra Bilirubin Total (K951595)	Modified Cobas Integra Bilirubin Total
Expected Values	Adults and infants >1month 3 4–17 umol/L (0 2 –1 0 mg/dL) Newborns (up to 24 h) 34-103 umol/L (2 0 – 6 0 mg/dL) Newborns (up to 48 h) 103-171 umol/L (6 0 -10 0 mg/dL) Newborns (3 to 5 days) 68 – 137 umol/L (4 0 – 8 0 mg/dL) Note It is recommended that each laboratory establishes and maintains its own reference ranges and that the values given here are used as a guideline only	Same Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference range

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Characteristic	Predicate Cobas Integra Bilirubin Total (K951595)	Modified Cobas Integra Bilirubin Total
Limitations – interference	Hemolysis Avoid hemolyzed specimens Even slight hemolysis interferes with the test Lipemia Avoid lipemic specimens Even slight lipemia interferes with the test Drugs Of the drugs tested in vitro, propranolol and theophyline cause artificially low total bilirubin values at the tested drug level	Hemolysis No significant interference up to an H index of 10 (approximate hemoglobin concentration 6 umol/L or 10 mg/dL) Lipemia (Intralipid)· No significant interference up to an L index of 9 There is a poor correlation between the L index (corresponds to turbidity) and triglycerides concentration Drugs Therapeutic drug interference was tested according to the recommendations of VDGH No interference was found Exception Propranolol and theophylline cause artificially low total bilirubin values at the tested drug level Hydroxocobalamin (Cyanokit) may cause false-high results Other In very rare cases gammopathy, in particular type IgM (Waldenstroms macroglobulinemia) may cause unreliable results

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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JAN 16 2009

Roche Diagnostics
c/o Jennifer Tribbett
Regulatory Affairs Principal
9115 Hague Road
Indianapolis, IN 46250

Re k081193
Trade/Device Name Roche COBAS Integra Bilirubin Total (BIL-T)
Regulation Number 21 CFR 862 1110
Regulation Name Bilirubin (total or direct) test system
Regulatory Class Class II
Product Code CIG
Dated December 18, 2008
Received December 19, 2008

Dear Ms Tribbett

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA) You may, therefore, market the device, subject to the general controls provisions of the Act The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895 In addition, FDA may publish further announcements concerning your device in the Federal Register

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies You must comply with all the Act's requirements, including, but not limited to registration and listing (21 CFR Part 807), labeling (21 CFR Parts 801 and 809), and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820)

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084 Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807 97) You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http //www fda gov/cdrh/dsma/dsmamain html

Sincerely yours,

Courtney C Harper, Ph D
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Indication for Use

510(k) Number (if known) K081193

Device Name **Roche COBAS Integra Bilirubin Total (BIL-T)**

Indication For Use

In vitro test for the quantitative determination of the total bilirubin concentration in human serum on COBAS Integra systems

Measurement of the level of bilirubin is used in the diagnosis and treatment of liver, hemolytic hematological, and metabolic disorders, including hepatitis and gall bladder block

Prescription Use XXX (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____ (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE, CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Carol C. Benson

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K081193